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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/809,029	03/16/2001	Martin C. Barnardo	1181-251	5589

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EXAMINER	
COUNTS, GARY W	

ART UNIT	PAPER NUMBER
1641	

NOTIFICATION DATE	DELIVERY MODE
09/07/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	09/809,029	BARNARDO ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9-17,20,22,24-27 and 29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9-17,20,22,24-27 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

The amendment filed June 20, 2007 is acknowledged and has been entered.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-7, 9-17, 20 , 22, 24, 25 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chang et al (US 5,270,169) in view of Walter et al., (Stimulation of human cytotoxic T cells with HIV-1-derived peptides presented by recombinant HLA-A2 peptide complexes, International Immunology, vol. 9, No. 3, pp. 451-459, 1997).

Chang et al disclose detecting the presence of anti-HLA antibodies. Chang et al disclose that the detection can be of antibodies to al least one HLA allele (col 2, lines 15-20) Chang et al disclose combining HLA antigens with a biological sample to form a complex (col 2, lines 1-11, col 3, lines 47-64). Chang et al disclose that the biological sample can be a body fluid (col 2). Chang et al disclose that the HLA antigen may be a synthetic HLA antigen (col 3, lines 60-63). Chang et al disclose attaching the molecules to a solid support such as a microtiter plate, beads or nitrocellulose (col 3, lines 1-19). Chang et al teaches the assay can be an ELISA performed in a microtiter plate (col 5, line 45 – col 6, line 37). Chang et al disclose that any convenient, accurate method may be employed for the detection of the surface bound complexes (col 4). Chang et al disclose comprising the reagents and components into a kit (col 5).

Chang et al differ from the instant invention in failing to specifically teach the HLA antigen is a recombinant HLA antigen.

Walter et al., disclose detecting a monoclonal PA2.1 antibodies (specific for HLA-A2 and A28). Walter et al disclose that this antibody binds to recombinant HLA-A2 peptide complexes. Walter et al disclose detecting the PA2.1 antibodies bound to the A2 complex with goat anti-mouse Ig conjugated to horseradish peroxidase (p. 452).

Walter et al disclose that the HLA-A2 molecule is produced in E.Coli (prokaryotic expression system) (p. 451). Walter et al disclose the recombinant molecule can be immobilized and bound by antibody (p. 456, first column, lines 43 – 53). Walter et al disclose assembling the HLA-A2 (HLA-A*001) heavy chain and B_2-microglobuling in the presence of a peptide from gag protein (Gag, amino acids 77086, SLYNTVATL) (It is note that this recombinant molecule appears to be the same recombinant molecule as disclosed by applicant (see page 23, Table 1). Walter et al disclose labeled antibodies that bind to the PA2.1 antibodies. Walter et al teaches that the recombinant complexes contain native epitopes, consistent with the presence of correctly folded molecular complexes (p.456, 2nd col).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate a recombinant HLA antigen and the corresponding reagents as taught by Walter et al into the method of Chang et al because Chang et al teaches that the HLA antigen can be a synthetic HLA antigen and Walter shows that recombinant HLA antigens can be used to detect allele specific antibodies and that the recombinant complexes contain native epitopes, consistent with the presence of correctly folded molecular complexes. Therefore, one of ordinary skill would have a reasonable expectation of success incorporating recombinant HLA antigens as taught by Walter et al into the method of Chang.

5. Claims 24-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chang et al in view of Walter et al as applied to claims 1-7, 9-17, 20 and 22-24 above, and further in view of Luxembourg et al.

See above for teachings of Chang et al and Walter et al.

Chang et al and Walter et al differ from the instant invention in failing to teach the MHC or HLA molecule is fused to biotin.

Luxembourg et al disclose recombinant MHC molecules which are biotinylated (page 3, paragraph 0018, & page 4, paragraph 0027). Luxembourg et al disclose that these recombinant MHC molecules are biotinlyated to provide attachment to solid support coated with avidin. Luxemburg et al disclose that the use of this avidin-biotin system provides for the isolation of peptides such as antibodies (p. 5, paragraphs 0030, and 0031).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate an avidin-biotin system as taught by Luxembourg et al into the modified method of Chang et al because Luxembourg et al shows that the use of this avidin-biotin system provides for the isolation of peptides such as antibodies. Further, the use of avidin-biotin systems to immobilize and capture reagents is very well known in the art. Therefore, one of ordinary skill in the art would have a reasonable expectation of success incorporating avidin-biotin as taught by Luxembourg et al into the modified method of Chang et al.

Response to Arguments

6. Applicant's arguments filed June 20, 2007 have been fully considered but they are not persuasive.

7. Applicant argues that one skilled in the art would not have any reason to combine Chang and Walter period, let alone arrive at something remotely similar to the present

claims. Walter is directed to the stimulation of human cytotoxic T cells with HIV-1 derived peptides presented by recombinant HLA-A2 peptide-bead complexes, essentially the creation of an HIV vaccine or therapy. Applicant states that Walter does not suggest a sample detection assay from a biological specimen similar to that described in Chang, who uses of HLA antigens in the formation of immune complexes that are subsequently detected by C1q moieties described above. Applicant argues that the only true rationale for combining Chang and Walter to arrive at anything remotely similar to the present claims is grounded firmly in hindsight reconstruction. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In the instant case as disclosed above and in the previous office action Chang et al specifically teaches that the HLA antigen can be a synthetic HLA antigen and Walter shows that recombinant HLA antigens (synthetic HLA antigens) can be used to detect allele specific antibodies and that the recombinant complexes contain native epitopes, consistent with the presence of correctly folded molecular complexes.

Applicant argues that correct complex formation is critical in Chang and it is highly unlikely that one would want to functionalize the HLA antigens with a solid support or

antibody, especially according to the aforementioned nonselective immobilization techniques in Walter, which could at best attenuate or alter if not altogether block the formation of complexes for C1q binding. This is not found persuasive because the arguments of counsel cannot take the place of evidence in the record. *In re Schulze,* 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965) (see MPEP 716.01(c)). Further, applicant's claims contain comprising language which does not exclude the addition of other components in the method.

Applicant argues that Chang et al and Walter et al fail to render claims 1-7,9-17, 20 and 22-24 and that Luxemburg does nothing to cure their deficiencies. This is not found persuasive because as stated above it is the Examiner's position that the one of ordinary skill in the art would combine Chang et al and Walter et al and the combination with Luxembourg et al renders obvious the claims 24-28, absent evidence to the contrary.

Applicant further states that claims 13 and 19 involve attachment of the MHC molecule to an ELISA plate and that in each of the cited references, binding of the HLA antigen to an ELISA plate would render them inoperable for their intended purpose. This is not found persuasive because the arguments of counsel cannot take the place of evidence in the record. *In re Schulze,* 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965) (see MPEP 716.01(c)).

Conclusion

8. No claims are allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gary Counts
Examiner
Art Unit
August 29, 2007

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